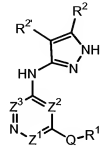
Amendments to the Claims

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claim 1 (Previously presented): A compound of formula **III**:



III

or a pharmaceutically acceptable salt thereof, wherein:

Z^1 is nitrogen or CR^8, Z^2 is CH, and Z^3 is nitrogen or CR^x, provided that when one of Z^1 or Z^3 is nitrogen, the other of Z^1 or Z^3 is CR^8 or CR^x, respectively;

R^x is $T\text{-}R^3$ or $L\text{-}Z\text{-}R^3$;

Q is selected from $-N(R^4)-$, -O-, –S-, or $-CH(R^6)-$;

R^1 is T-(Ring D);

Ring D is a 5-7 membered monocyclic ring or 8-10 membered bicyclic ring selected from aryl, heteroaryl, heterocyclyl or carbocyclyl, said heteroaryl or heterocyclyl ring having 1-4 ring heteroatoms selected from nitrogen, oxygen or sulfur, wherein each substitutable ring carbon of Ring D is independently substituted by oxo, $T\text{-}R^5$, or $V\text{-}Z\text{-}R^5$, and each substitutable ring nitrogen of Ring D is independently substituted by $-R^4$;

T is a valence bond or a $C_{1\text{-}4}$ alkylidene chain, wherein when Q is $-CH(R^6)-$, a methylene unit of said $C_{1\text{-}4}$ alkylidene chain is optionally replaced by -O-, -S-, $-N(R^4)-$, -CO-, -OC(O)NH-, or $-NHCO_2-$;

Z is a $C_{1\text{-}4}$ alkylidene chain;

L is $-O-$, $-S-$, $-SO-$, $-SO_2-$, $-N(R^6)SO_2-$, $-SO_2N(R^6)-$, $-N(R^6)-$, $-CO-$, $-CO_2-$, $-N(R^6)CO-$, $-N(R^6)C(O)O-$, $-N(R^6)CON(R^6)-$, $-N(R^6)SO_2N(R^6)-$, $-N(R^6)N(R^6)-$, $-C(O)N(R^6)-$, $-OC(O)N(R^6)-$, $-C(R^6)_2O-$, $-C(R^6)_2S-$, $-C(R^6)_2SO-$, $-C(R^6)_2SO_2-$, $-C(R^6)_2SO_2N(R^6)-$, $-C(R^6)_2N(R^6)-$,

$-C(R^6)_2N(R^6)C(O)-$, $-C(R^6)_2N(R^6)C(O)O-$, $-C(R^6)=NN(R^6)-$, $-C(R^6)=N-O-$, $-C(R^6)_2N(R^6)N(R^6)-$, $-C(R^6)_2N(R^6)SO_2N(R^6)-$, or $-C(R^6)_2N(R^6)CON(R^6)-$;

R^2 and $R^{2'}$ are independently selected from -R, -T-W-R^6, or R^2 and $R^{2'}$ are taken together with their intervening atoms to form a fused, 5-8 membered, unsaturated or partially unsaturated, ring having 0-3 ring heteroatoms selected from nitrogen, oxygen, or sulfur, wherein each substitutable ring carbon of said fused ring formed by R^2 and $R^{2'}$ is independently substituted by halo, oxo, -CN, $-NO_2$, -R^7, or -V-R^6, and each substitutable ring nitrogen of said ring formed by R^2 and $R^{2'}$ is independently substituted by R^4;

R^3 is selected from -R, -halo, -OR, $-C(=O)R$, $-CO_2R$, -COCOR, $-COCH_2COR$, $-NO_2$, -CN, $-S(O)R$, $-S(O)_2R$, -SR, $-N(R^4)_2$, $-CON(R^7)_2$, $-SO_2N(R^7)_2$, $-OC(=O)R$, $-N(R^7)COR$, $-N(R^7)CO_2(C_{1\text{-}6}$ aliphatic), $-N(R^4)N(R^4)_2$, $-C=NN(R^4)_2$, $-C=N-OR$, $-N(R^7)CON(R^7)_2$, $-N(R^7)SO_2N(R^7)_2$, $-N(R^4)SO_2R$, or $-OC(=O)N(R^7)_2$;

each R is independently selected from hydrogen or an optionally substituted group selected from $C_{1\text{-}6}$ aliphatic, $C_{6\text{-}10}$ aryl, a heteroaryl ring having 5-10 ring atoms, or a heterocyclyl ring having 5-10 ring atoms;

each R^4 is independently selected from $-R^7$, $-COR^7$, $-CO_2$(optionally substituted $C_{1\text{-}6}$ aliphatic), $-CON(R^7)_2$, or $-SO_2R^7$;

each R^5 is independently selected from -R, halo, -OR, $-C(=O)R$, $-CO_2R$, -COCOR, $-NO_2$, -CN, $-S(O)R$, $-SO_2R$, -SR, $-N(R^4)_2$, $-CON(R^4)_2$, $-SO_2N(R^4)_2$, $-OC(=O)R$, $-N(R^4)COR$, $-N(R^4)CO_2$(optionally substituted $C_{1\text{-}6}$ aliphatic), $-N(R^4)N(R^4)_2$, $-C=NN(R^4)_2$, $-C=N-OR$, $-N(R^4)CON(R^4)_2$, $-N(R^4)SO_2N(R^4)_2$, $-N(R^4)SO_2R$, or $-OC(=O)N(R^4)_2$;

V is -O-, -S-, -SO-, $-SO_2-$, $-N(R^6)SO_2-$, $-SO_2N(R^6)-$, $-N(R^6)-$, -CO-, $-CO_2-$, $-N(R^6)CO-$, $-N(R^6)C(O)O-$, $-N(R^6)CON(R^6)-$, $-N(R^6)SO_2N(R^6)-$, $-N(R^6)N(R^6)-$, $-C(O)N(R^6)-$, $-OC(O)N(R^6)-$, $-C(R^6)_2O-$, $-C(R^6)_2S-$, $-C(R^6)_2SO-$, $-C(R^6)_2SO_2-$, $-C(R^6)_2SO_2N(R^6)-$, $-C(R^6)_2N(R^6)-$, $-C(R^6)_2N(R^6)C(O)-$, $-C(R^6)_2N(R^6)C(O)O-$, $-C(R^6)=NN(R^6)-$, $-C(R^6)=N-O-$, $-C(R^6)_2N(R^6)N(R^6)-$, $-C(R^6)_2N(R^6)SO_2N(R^6)-$, or $-C(R^6)_2N(R^6)CON(R^6)-$;

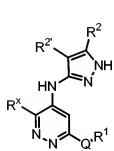
W is $-C(R^6)_2O-$, $-C(R^6)_2S-$, $-C(R^6)_2SO-$, $-C(R^6)_2SO_2-$, $-C(R^6)_2SO_2N(R^6)-$, $-C(R^6)_2N(R^6)-$, -CO-, $-CO_2-$, $-C(R^6)OC(O)-$, $-C(R^6)OC(O)N(R^6)-$, $-C(R^6)_2N(R^6)CO-$, $-C(R^6)_2N(R^6)C(O)O-$, $-C(R^6)=NN(R^6)-$, $-C(R^6)=N-O-$, $-C(R^6)_2N(R^6)N(R^6)-$, $-C(R^6)_2N(R^6)SO_2N(R^6)-$, $-C(R^6)_2N(R^6)CON(R^6)-$, or $-CON(R^6)-$;

each R^6 is independently selected from hydrogen or an optionally substituted C_{1-4} aliphatic group, or two R^6 groups on the same nitrogen atom are taken together with the nitrogen atom to form a 5-6 membered heterocyclyl or heteroaryl ring;

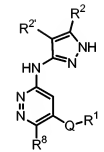
each R^7 is independently selected from hydrogen or an optionally substituted C_{1-6} aliphatic group, or two R^7 on the same nitrogen are taken together with the nitrogen to form a 5-8 membered heterocyclyl or heteroaryl ring; and

R^8 is selected from -R, halo, -OR, -C(=O)R, -CO_2R, -COCOR, -NO_2, -CN, -S(O)R, -SO_2R, -SR, -$N(R^4)_2$, -$CON(R^4)_2$, -$SO_2N(R^4)_2$, -$OC(=O)R$, -$N(R^4)COR$, -$N(R^4)CO_2$(optionally substituted C_{1-6} aliphatic), -$N(R^4)N(R^4)_2$, -$C{=}NN(R^4)_2$, -$C{=}N$-OR, -$N(R^4)CON(R^4)_2$, -$N(R^4)SO_2N(R^4)_2$, -$N(R^4)SO_2$R, or -$OC(=O)N(R^4)_2$.

Claim 2 (Previously presented): The compound according to claim 1, wherein Q is -$N(R^4)$-, -S-, or -$CH(R^6)$-, and said compound is of formula **IIIa** or **IIIb**



IIIa



IIIb

or a pharmaceutically acceptable salt thereof.

Claim 3 (Previously presented): The compound according to claim 2, wherein one or more compound variables are selected from the group consisting of:

(a) R^x is hydrogen, alkyl- or dialkylamino, acetamido, or a C_{1-4} aliphatic group;

(b) R^1 is T-(Ring D), wherein T is a valence bond or a methylene unit;

(c) Ring D is a 5-7 membered monocyclic or an 8-10 membered bicyclic aryl or heteroaryl ring; and

(d) R^2 is –R or –T-W-R^6 and $R^{2'}$ is hydrogen, or R^2 and $R^{2'}$ are taken together to form an optionally substituted benzo ring.

Claim 4 (Original): The compound according to claim 3, wherein:

(a) R^x is hydrogen, alkyl- or dialkylamino, acetamido, or a C_{1-4} aliphatic group;

(b) R^1 is T-(Ring D), wherein T is a valence bond or a methylene unit;

(c) Ring D is a 5-7 membered monocyclic or an 8-10 membered bicyclic aryl or heteroaryl ring; and

(d) R^2 is –R or –T-W-R^6 and $R^{2'}$ is hydrogen, or R^2 and $R^{2'}$ are taken together to form an optionally substituted benzo ring.

Claim 5 (Previously presented): The compound according to claim 3, wherein one or more compound variables selected from the group consisting of:

(a) R^1 is T-(Ring D), wherein T is a valence bond, and Q is -S- or -NH-;

(b) Ring D is a 5-6 membered monocyclic or an 8-10 membered bicyclic aryl or heteroaryl ring; and

(c) R^2 is –R and $R^{2'}$ is hydrogen, wherein R is selected from hydrogen, C_{1-6} aliphatic, phenyl, a 5-6 membered heteroaryl ring, or a 5-6 membered heterocyclic ring.

Claim 6 (Original): The compound according to claim 5, wherein:

(a) R^1 is T-(Ring D), wherein T is a valence bond, and Q is -S- or -NH-;

(b) Ring D is a 5-6 membered monocyclic or an 8-10 membered bicyclic aryl or heteroaryl ring; and

(c) R^2 is -R and $R^{2'}$ is hydrogen, wherein R is selected from hydrogen, C_{1-6} aliphatic, phenyl, a 5-6 membered heteroaryl ring, or a 5-6 membered heterocyclic ring.

Claim 7 (Previously presented): The compound according to claim 5, wherein one or more compound variables are selected from the group consisting of:

(a) R^x is hydrogen methyl, ethyl, propyl, cyclopropyl, isopropyl, methylamino or acetamido;

(b) R^1 is T-(Ring D), wherein T is a valence bond and Ring D is a 5-6 membered aryl or heteroaryl ring, wherein Ring D is optionally substituted with one to two groups selected from -halo, -CN, -NO_2, -$N(R^4)_2$, optionally substituted C_{1-6} aliphatic group, -OR, -CO_2R, -$CON(R^4)_2$, -$OCO(R^4)_2$, -$N(R^4)COR$, -$N(R^4)SO_2R$, -$N(R^6)COCH_2CH_2N(R^4)_2$, or -$N(R^6)COCH_2CH_2CH_2N(R^4)_2$; and

(c) R^2 is hydrogen or a substituted or unsubstituted C_{1-6} aliphatic.

Claim 8 (Original): The compound according to claim 7, wherein:

(a) R^x is hydrogen methyl, ethyl, propyl, cyclopropyl, isopropyl, methylamino or acetamido;

(b) R^1 is T-(Ring D), wherein T is a valence bond and Ring D is a 5-6 membered aryl or heteroaryl ring, wherein Ring D is optionally substituted with one to two groups selected from -halo, -CN, $-NO_2$, $-N(R^4)_2$, optionally substituted C_{1-6} aliphatic group, -OR, $-CO_2R$, $-CON(R^4)_2$, $-OCO(R^4)_2$, $-N(R^4)COR$, $-N(R^4)SO_2R$, $-N(R^6)COCH_2CH_2N(R^4)_2$, or $-N(R^6)COCH_2CH_2CH_2N(R^4)_2$; and

(c) R^2 is hydrogen or a substituted or unsubstituted C_{1-6} aliphatic.

Claim 9 (Previously presented): A compound selected from the group consisting of:

N^5-(1*H*-Indazol-6-yl)-N^3-(5-methyl-1*H*-pyrazol-3-yl)-pyridazine-3,5-diamine;

N-{4-[6-(5-Methyl-1*H*-pyrazol-3-ylamino)-pyridazin-4-ylsulfanyl]-phenyl}-acetamide;

[5-(3-Methoxy-benzyl)-pyridazin-3-yl]-(5-methyl-1*H*-pyrazol-3-yl)-amine;

N^3-(5-Cyclopropyl-1*H*-pyrazol-3-yl)-N^5-pyridin-3-ylmethyl-pyridazine-3,5-diamine;

[5-(Benzothiazol-6-ylsulfanyl)-pyridazin-3-yl]-(5-cyclopropyl-1*H*-pyrazol-3-yl)-amine;

{4-[6-(5-Cyclopropyl-1*H*-pyrazol-3-ylamino)-pyridazin-4-yloxy]-phenyl}-acetonitrile;

N-{4-[6-(1*H*-Indazol-3-ylamino)-pyridazin-4-ylamino]-phenyl}-methanesulfonamide;

(1*H*-Indazol-3-yl)-[5-(thiophen-2-ylmethylsulfanyl)-pyridazin-3-yl]-amine;

N^5-(5-Methyl-1*H*-pyrazol-3-yl)-N^3-pyridin-3-ylmethyl-pyridazine-3,5-diamine;

[6-(Benzothiazol-6-ylsulfanyl)-pyridazin-4-yl]-(5-methyl-1*H*-pyrazol-3-yl)-amine;

{4-[5-(5-Methyl-1*H*-pyrazol-3-ylamino)-pyridazin-3-yloxy]-phenyl}-acetonitrile;

N^5-(5-Cyclopropyl-1*H*-pyrazol-3-yl)-N^3-(1*H*-indazol-6-yl)-pyridazine-3,5-diamine;

N-{4-[5-(5-Cyclopropyl-1*H*-pyrazol-3-ylamino)-pyridazin-3-ylsulfanyl]-phenyl}-acetamide;

N^5-(1*H*-Indazol-3-yl)-N^3-(1*H*-indazol-6-yl)-pyridazine-3,5-diamine; and

(1*H*-Indazol-3-yl)-[6-(3-methoxy-phenylsulfanyl)-pyridazin-4-yl]-amine.

Claim 10 (Original): A composition comprising a compound according to any of claims 1-9, and a pharmaceutically acceptable carrier.

Claim 11 (Original): The composition according to claim 10, further comprising an additional therapeutic agent.

Claim 12-20 (Cancelled)

Claim 21 (Original): A method of treating diabetes, which method comprises administering to a patient in need of such a treatment a therapeutically effective amount of a composition according to claim 10.

Claims 22-24 (Cancelled)

Claim 25 (Original): A method of treating Alzheimer's disease by inhibiting the production of hyperphosphorylated Tau protein in a patient, which method comprises administering to a patient in need thereof a therapeutically effective amount of a composition according to claim 10.

Claim 26 (Cancelled)

Claim 27 (Presently amended): A method of lowering blood levels of glucose in a patient in need thereof, which method comprises administering to said patient a therapeutically effective amount of a compound according to any one of claims 1-9~~ or a composition according to claim 10~~.

Claim 28 (Presently amended): A method of treating schizophrenia, which method comprises administering to a patient in need thereof a therapeutically effective amount of a compound according to any one of claims 1-9~~ or a composition according to claim 10~~.

Claim 29 (Presently amended): A method of treating Alzheimer's disease, which method comprises administering to a patient in need thereof a therapeutically effective amount of a compound according to any one of claims 1-9~~ or a composition according to claim 10~~.

Claim 30 (Presently amended): A method of treating a disorder of the central nervous system, which method comprises administering to a patient in need thereof a therapeutically effective amount of a compound according to any one of claims 1-9~~ or a composition according to claim 10~~.

Claim 31 (Original): The method of claim 30, wherein the disorder of the central nervous system is selected from the group consisting of manic depressive disorder, neurodegenerative diseases, and cardiomyocete hypertrophy.

Claim 32 (New): A method of lowering blood levels of glucose in a patient in need thereof, which method comprises administering to said patient a therapeutically effective amount of a compound according to a composition according to claim 10.

Claim 33 (New): A method of treating schizophrenia, which method comprises administering to a patient in need thereof a therapeutically effective amount of a compound according to a composition according to claim 10.

Claim 34 (New): A method of treating Alzheimer's disease, which method comprises administering to a patient in need thereof a therapeutically effective amount of a compound according to a composition according to claim 10.

Claim 35 (New): A method of treating a disorder of the central nervous system, which method comprises administering to a patient in need thereof a therapeutically effective amount of a compound according to a composition according to claim 10.

Claim 36 (New): The method of claim 35, wherein the disorder of the central nervous system is selected from the group consisting of manic depressive disorder, neurodegenerative diseases, and cardiomyocete hypertrophy.